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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,018	01/31/2005	Yoshiharu Minamitake	58778.000002	9040

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EXAMINER	
TSAY, MARSHA M	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,018	MINAMITAKE ET AL	
	Examiner	Art Unit	
	Marsha M. Tsay	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending and under examination.

Priority: The current application was filed January 31, 2005. This application is a 371 of PCT/JP03/04590, filed April 10, 2003, which in turn claims priority to JP 2002109761, filed April 11, 2002. The priority date, in terms of earliest filing date, is April 11, 2002.

Claim Objections

Claims 8, 12, 16-18, 22-23 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot refer back to another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-7, 13-15, 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is drawn to a sub-step (d) wherein a peptide fragment is cleaved from the weak acid-cleavable resin without elimination of the protecting group in the peptide

fragment. However, in sub-step (b), the protecting group has been removed or deprotected and modified with a substituent R (c). It is unclear if the protecting group in the peptide fragment is still present or has been deprotected.

Claim 3 is drawn to Japanese characters that are in parenthesis. These terms should be deleted or translated and rewritten into English.

Claims 4-7 are included in this rejection because they are dependent on claim 3.

Claims 13-15, 19-21 are drawn to a protected peptide fragment containing no modified amino acid or non-amino acid. The peptide fragment cannot be protected without modifying at least one amino acid in the peptide fragment.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 9, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Kitagawa et al. (2001 Chem. Pharm. Bull. 49(8): 958-963; listed on Applicant's IDS). Kitagawa et al. teach the facile solid-phase synthesis of sulfated tyrosine-containing peptides, notably, human big gastrin-II and its c-terminal glycine-extended (G34-Gly Sulfate) by the solid-phase segment condensation approach. Kitagawa et al. teach the sequence of big gastrin-II was divided into four peptide segments and that 2-chlorotrityl (Clt) resin was exclusively employed for the preparation of the peptide segments (p. 959, chart 1). The C-terminal resin-bound segment [1a] containing a Tyr(SO_3H) residue

was constructed on Fmoc-Asp(Clt resin)-Phe-NH_2. Kitagawa et al. teach the β-carboxyl group of the Asp residue was used to form an acid-labile ester linkage between the C-terminal dipeptide amide and a Clt resin (p. 959, 2nd paragraph). Kitagawa et al. teach the peptide chain [1a] was elongated manually according to general procedures of Fmoc-based solid phase protein synthesis, and the Tyr(SO_3H) residue was introduced using Fmoc-Tyr(SO_3Na)-OH as a building block. The remaining big gastrin-II peptide segments [2]-[4] were constructed on H-Pro-Clt resin according to the general procedures of Fmoc-based solid phase protein synthesis and then segment condensations took place directly on the resin-bound segment [1a] (p. 959, 3rd paragraph). Kitagawa et al. teach the preparation of segments [2] and [3] with 'Buc and Boc protecting groups. On p. 960, chart 2, Kitagawa et al. teach segment [2] was detached from the Clt resin using HFIP/CH_2Cl without disturbing the 'Buc-Ser and Boc-Lys blocking groups. Kitagawa et al. teach the segment condensation of segments [1a]-[4] was promoted by a PyBOP-mediated coupling protocol [PyBOP-reagent, *N*-hydroxybenzotriazole (HOBt), *N*-methylmorpholine (NMM) (p. 960, 2nd paragraph; claims 9, 11).

Claims 1-2, 5-7, 12-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Kangawa et al. (EP 1197496; listed on Applicant's IDS). In example 10 (p. 41), Kangawa et al. teach the synthesis of various ghrelin derivatives. Under this experimental section, Kangawa et al. teach the synthesis of a ghrelin derivative, compound 9, having acyl serine or acyl threonine (Boc method) (p. 44, line 24; claim 1,

2, 5, 7). Kangawa et al. teach protected rat ghrelin resin (4-28) was constructed from Boc-Arg (Tos)-Pam resin by Boc chemistry, and Boc-Ser ($CO\text{-}CH_2CH_3$)-OH, Boc-Ser (Bzl)-OH and Boc-Gly-OH were condensed with a half (1.4g) of the resin. The protected peptide resin was deprotected with anhydrous hydrogen fluoride (HF) in the presence of p-cresol thereby releasing the peptide, which was then purified.

Furthermore, Kangawa et al. teach several substitution groups that can be used in modifying the side chain of the third serine of the ghrelin derivative peptide-type compounds synthesized from example 10. In Tables 4-10, Kangawa et al. teach the effects of different side groups that are linked at the third serine of selected ghrelin derivative peptide-type compounds (p. 52-58, claim 1-2, 5-7). In addition, Kangawa et al. teach the mode of linkage of a side chain at the third serine is an ester linkage (p. 59, line 44, claim 6). In their claims, especially claims 49-53, Kangawa et al. also teach a method for producing a ghrelin peptide-type compound by genetic recombination technology which comprises transforming a vector containing a DNA encoding a ghrelin derivative into host cells, culturing the resulting transformed cells, recovering the desired ghrelin peptide-type compound from the culture, followed by chemically modifying an amino acid (p. 101, line 18-21; claim 12-13). The genetic recombination technology comprises using cells having the activity of binding a fatty acid via an ester linkage to a side-chain hydroxyl group of an amino acid or via a thioester linkage to a side-chain mercapto group of an amino acid in the peptide-type compound (p. 101, lines 23-26; claim 12-13).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitagawa et al. (2001 Chem. Pharm. Bull. 49(8): 958-963). Kitagawa et al. disclose the general procedure of Fmoc-Based solid phase protein synthesis. Each peptide segment [1a], [2]-[3] of human big gastrin-II was synthesized by this general procedure (chart 1). The coupling reaction that incorporated each subsequent amino acid into the peptide segment was promoted in DMF by a DIPCDI-HOBt coupling protocol or a PyBOP-mediated coupling protocol (p. 961). Further in their experiment, Kitagawa et al. disclose the condensation of the peptide segments was promoted by a PyBOP-mediated coupling protocol. Kitagawa et al. do not teach the condensation of peptide fragments by the DIPCDI-HOBt coupling protocol.

It would have been obvious to a person having ordinary skill in the art to prepare a peptide fragment protected by Boc on a Lys residue (claim 1a), prepare another peptide segment without the presence of a protecting group (claim 1b) and join the two peptide segments together by a DIPCDI-HOBt coupling protocol (claim 9-11) because Kitagawa et al. teach the preparation of segment [1a] of human big gastrin-II without a Boc protecting group on Clt resin, the preparation of a segment [2] with a Boc protecting group on Clt resin, and the condensation of the two segments. Although Kitagawa et al.

do not use the same condensing agent as the instant claims 9-11, they disclose that both the DIPCDI-HOBt coupling protocol or a PyBOP-mediated coupling protocol have the same mechanism.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 18, 2005

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER